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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/641,081	08/16/2000	Carsten Rosenow	3334.2	3725
54947	7590	06/23/2006		
MICHAELSON & ASSOCIATES P.O. BOX 8489 328 NEWMAN SPRINGS, PARKWAY 109 OFFICE CENTER RED BANK, NJ 07701-8489			EXAMINER ZHOU, SHUBO	
			ART UNIT 1631	PAPER NUMBER

DATE MAILED: 06/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/641,081

Applicant(s)

ROSENOW ET AL.

Examiner

Shubo (Joe) Zhou

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 December 2005 and 05 April 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants' amendment and request for reconsideration in the communication filed on 12/13/05 and 4/5/06 are acknowledged and the amendments entered.

Applicant's arguments in response to the previous Office action have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous Office action are hereby withdrawn. The following rejections and/or objections are reiterated from the previous Office action, mailed 6/7/05, and constitute the complete set presently being applied to the instant application.

Claims 1-9 are currently pending and under consideration.

Withdrawn Rejection

2. The rejections of claims 1-9 under 35 U.S.C. 112 , second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention set forth in the previous Office action mailed 6/7/05 is hereby withdrawn in view of the claim amendments to the claims filed 12/13/05.

Claim Rejections-35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leary et al. (WO 99/67422, 29 December 1999) in view of Lockhart et al. (WO 97/10365, 20 March 1997).

The claims are drawn to a method of identifying a transcribed region in a genome comprising hybridizing probes to transcripts from a genome and identifying a transcribed region if the hybridization signal between a probe and a transcript is above a threshold value.

Leary et al. disclose a method for mapping the position of individual transcripts from a genome comprising hybridizing a plurality of nucleic acid probes with a nucleic acid sample wherein the sample comprises transcripts from the genome and the probes are from an area of the genome (page 4, first paragraph) and such probes are immobilized to a substrate (pages 7-8, the bridging paragraph). Leary et al. also disclose that the probes for hybridization are overlapping probes from a genomic region. See page 5. Leary et al. do not explicitly recite a threshold value for the hybridization signal of a region, above which, the region would be considered as transcribed.

Lockhart et al. teach a method of monitoring gene expression by hybridization of

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transcripts to high density oligonucleotide arrays. The method comprises hybridizing test transcripts to genomic probes immobilized onto substrates (page 3, Summary of the invention). To reduce the signal/noise ratio, Lockhart et al. teach using different control probes including normalization controls, expression level controls and mismatch control (pages 6-7 and 34-35).

Lockhart et al. state (page 39):

The oligonucleotide array is hybridized to a sample containing target nucleic acids having subsequences complementary to the oligonucleotide probes and the difference in hybridization intensity between each probe and its mismatch control is determined. Only those probes where the difference between the probe and its mismatch control exceeds a threshold hybridization intensity (e.g. preferably greater than 10% of the background signal intensity, more preferably greater than 20% of the background signal intensity and most preferably greater than 50% of the background signal intensity) are selected.

A person having ordinary skill in the art at the time the invention was made would therefore have been motivated by Lockhart et al. to modify Leary et al. to include all the control probes including the mismatch probes and to use a threshold with each control probe as suggested by Lockhart et al. in order to reduce the signal/noise ratio.

As to claims 2 and 3, Leary et al. disclose that the probes of the genomic fragments can be oligonucleotides of 20 or more bases long to be immobilized onto a substrate (page 9, last paragraph, and the bridging paragraph of pages 7-8).

As to claims 4-5, Lockhart et al. disclose that the mismatch probes used as control probes comprise one or more mismatch at the center of the oligonucleotides, and provide control for non-specific binding. See pages 36.

Claim 6 recites "identifying a sub-region wherein hybridization of said probes targeting said sub-region is similar, thereby indicating said sub-region as said transcribed region. Leary et al. describe in Figure 1 graphically the method of mapping a transcript to a genome. Linear and overlapping fragments were fixed onto a substrate as dots wherein the genomic location for each

dot is known. Transcripts from a sample are hybridized to the probes and similar patterns of hybridization, i.e. "bold" signals on the substrate, are considered as positive hybridization, indicating that the particular sub-regions represented by these genomic probes are transcribed.

As to claims 7 and 9, which recite bacteria and prokaryotes, Leary et al. disclose that the preferred embodiments in their method include using genomic fragments of bacterial species, most particularly a human pathogen such as *Streptococcus*, a prokaryote. See page 10, last paragraph.

This rejection is reiterated from the previous Office action mailed 6/7/05.

Applicants' arguments filed 12/13/05 have been fully considered but they are not persuasive. The argument is on the ground that neither Lockhart nor Leary teach or suggest the advantageous identification of a region in which all consecutive probes have above-threshold hybridization intensities. See page 8 of 9 of the response. This is not persuasive because Leary et al. clearly used overlapping probes immobilized on a substrate for transcript mapping. See page 5 and Fig. 1. It would be readily apparent to one skilled in the art that such overlapping probes are consecutive in the region of the genome.

5. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Leary et al. (WO 99/67422, 29 December 1999) in view of Lockhart et al. (WO 97/10365, 20 March 1997), as applied to claims 1-7 and 9 above, and further in view of Darnell et al. (Molecular Cell Biology, Scientific American Books, 1986).

Claim 8 is drawn to a method of identifying a transcribed region in a genome comprising hybridizing probes to transcripts from a genome and identifying a transcribed region if the hybridization signal between a probe and a transcript is above a threshold value. The claim recites that the transcribed region is an operon.

As applied to claims 1-7 and 9 above, the combination of Leary et al. and Lockhart et al. discloses a method of identifying a transcribed region in a genome comprising hybridizing probes to transcripts from a genome and identifying a transcribed region if the hybridization signal between a probe and a transcript is above a threshold value.

Leary et al. and Lockhart et al. do not teach identifying a transcribed region that is an operon.

However, Leary et al. teach mapping transcripts with the same 5' end to a viral genome. Leary et al. state that their method, referred to as "FAT", is particularly useful for identifying genes whose transcripts have common ends, and that genes are temporally regulated such as herpes simplex virus type I. See page 3.

Darnell et al. teach that operon are part of a genome from which a single transcript comprises multiple genes and the production of this transcript, i.e. transcription, is temporally regulated, e.g. the lactose operon regulated by the presence of lactose. See pages 284 and 285.

Given that the transcripts for each of the genes comprised in an operon can be interpreted as having common ends, and that Leary et al. motivate using their method for genes that are temporally regulated and for transcripts that have a common end, one having ordinary skill in the art at the time the invention was made would therefore have been motivated to modify Leary et al. to modify the methods of Leary et al. and Lockhart et al. to apply the methods for mapping transcripts to all genes whose transcription are temporally regulated and whose transcripts have common ends, such as those of an operon.

This rejection is reiterated from the previous Office action mailed 6/7/05.

Applicants' argument filed 4/5/06 has been fully considered but it is not persuasive. The argument is on the same ground as that presented for the rejection set forth in paragraph 4 above.

The argument is not deemed persuasive for the same reason as set forth above for the rejection set forth in paragraph 4.

Conclusion

6. No claim is allowed.

7. **THIS ACTION IS MADE FINAL.**

8. Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. §1.136


(a). A shortened statutory period for response to this final action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this final action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than six months from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

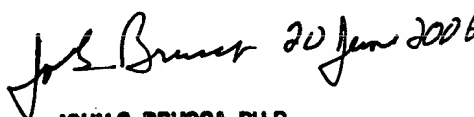
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Shubo (Joe) Zhou, Ph.D. 

Patent Examiner


JOHN S. BRUSCA, PH.D.
PRIMARY EXAMINER